July 1, 2002

Ms. Christine Todd Whitman, Administrator
U.S. EPA
P.O. Box 1473
Merrifield, VA 22116

Attn: Chemical Right-to-Know Program

RE: HPV Chemical Challenge Program, AR-201

Dear Ms. Whitman:

This letter is submitted by Eastman Chemical Company ("Eastman") in response to comments received from the Environmental Protection Agency ("EPA") dated June 28, 2002 following EPA's review of the test plan and robust summaries for 5-methyl-2-hexanone (methyl iso-amyl ketone, MIAK, CAS No.: 110-12-3). I would like to thank the EPA for its review and welcome the recognition of its completeness and fulfillment of Eastman's obligation to this chemical in the HPV program.

Below are the EPA's comments to various robust summaries and our responses:

Health Effects

1. *"Repeated-Dose Toxicity*. In both summaries, the submitter needs to define the specific tissues that were examined histopathologically."

The specific tissues harvested for histological examination have been added to the robust summaries.

2. *"Genetic Toxicity (in vitro)*. In both summaries, the submitter needs to list concentrations that were tested. The submitter also needs to provide the number of replicate plates per concentration for the reverse mutation in bacteria study and the number of metaphases per concentration that were examined for the chromosomal aberration assay."

The number of replicate plates and metaphases analyzed has been added to the respective robust summaries. As no evidence of genotoxicity was seen in either study and due to the fact that the studies were conducted following standard guidelines, we deem it adequate to list only the maximum concentration assessed. The EPA did not note this as criteria for completeness in other reviews on test plans previously submitted

Ecotoxicity

1. *"Fish and Invertebrates.* The fish and invertebrate toxicity studies were conducted at 100 µl/L and no effects were reported. Data for these two endpoints are inadequate because the loss of chemical during the test was not accounted for. The submitter needs to redo the fish and invertebrate toxicity tests. More information on testing volatile chemicals can be found in the Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures (OECD, June 2000 - available on the OECD website at http://www.oecd.org/ehs/test/monos.htm)."

Eastman disagrees that the data for fish and Daphnia are inadequate and need to be redone. While the test concentrations for MIAK were not measured, more recent daphnia and fish studies conducted with an isomeric ketone, methyl n-amyl ketone (MAK), indicated relatively low losses in comparisons of nominal versus measured concentrations(see table below and test plan for MAK, CAS No.:110-43-0).

MAK

Concentration (mg/ml)	Fish		Daphnia
Nominal:	0, 39.5, 60.8, 93.6, 144, 221		6.25, 12.5, 25, 50, 100
Measured:	0, 40.9, 58.3, 96.0, 147, 232		6.46, 13.01, 24.52, 47.86, 90.10

These data suggest that under the conditions used in the fish and daphnia assays significant loss was not observed with MAK and hence would also unlikely to have occurred with MIAK. The two chemicals, MIAK and MAK, are structural isomers and have essentially identical values for Henry's Law Constant. Furthermore, fugacity modeling predicts minimal distribution to the air phase. Thus, although the MIAK studies lacked a measurement of their actual exposure levels, they followed methods that were scientifically acceptable and robust for the date at which they were conducted (1978) and are well documented for their age. Both studies were deemed as "Reliable with restrictions". In addition, both the fish and daphnia studies for MIAK reported a No Observable Effect Concentration (NOEC) at the 100 uL/L concentration. This endpoint indicates that the material has less of a toxic effect than a material that reported a LC50 at the same concentration.

2. *"Algae*. Missing study details included number of replications performed, water hardness, and TOC."

The robust summary for this endpoint consisted of data on MIAK derived from the ECOSAR modeling program in conjunction with data from MAK used as a structural surrogate. MAK is also in the HPV program and the robust summary presented in the MIAK test plan was extracted from the MAK test plan that had already been reviewed and deemed adequate as written.

Environmental Fate

1. *"Fugacity*. The submitter needs to provide the inputs used for the transport and distribution model. EPA recommends that the submitter use the measured physicochemical data as inputs for the transport and distribution model. The use of estimated values introduces uncertainties that then become magnified in modeling applications."

The inputs used to derive the fugacity values found in the robust summary were default values chosen by the EPIWIN program. This is noted in the robust summary.

Enclosed with this letter is a computer diskette containing the test plan and modified robust summaries in Adobe Acrobat (.pdf) format. The HPV registration number for Eastman Chemical Company is 1100266.

Sincerely,

James A. Deyo, D.V.M., Ph.D., D.A.B.T.
Technical Associate

Enclosure